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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Francis Law Group
1942 Embarcadero
Oakland, CA 94606

EXAMINER

BORGEEST, CHRISTINA M

ART UNIT PAPER NUMBER

1649

DATE MAILED: 09/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/789,105

Applicant(s)

ROBERTS ET AL.

Examiner

Christina Borgeest

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on February 27, 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-17 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments or Claims

The preliminary amendments of 2/27/04 and 12/23/04 have been entered. Claims 1-17 are under examination. Applicant's attempt to claim 371 status is acknowledged, however, it is not proper for the following reasons: This is not a national stage application since there are conflicting instructions regarding the filing of this application. On the one hand, applicant filed an amendment to the specification on 27 Feb 2004 which indicated a national stage filing under 35 USC 371. However, applicant's transmittal letter filed 27 Feb 2004 indicates a filing of a nonprovisional application under 37 CFR 1.53(b). The last paragraph of MPEP 1893.03(a) indicates that an application will be treated as a filing under 35 USC 111(a) (regular nonprovisional application) if there are any conflicting instructions and even the use of Transmittal Form SB/05 (which this applicant used) will cause the application to be processed as a 111(a) application and not a 371 application.

Applicant should be able to designate this application as a "continuation" or "continuation-in-part" of the PCT application. See MPEP 1895. However, the time period for indicating this relationship under 37 CFR 1.78 has expired and the applicant would now need to file a petition under 1.78 in order to insert this continuity data.

Election/Restrictions

Restriction to one of the following Groups is required under 35 U.S.C. 121:

- I. Claims 1-7, drawn to a method of regulating cytotrophoblast differentiation and migration and/or promoting embryo implantation in the uterine decidua endometrium, comprising administration of a differentiation factor selected from the group consisting of: IGF-II, an IGF-II analogue, and a TGF-beta antibody, to promote interaction between IGFII and the cation independent mannose-6-phosphate (CIM6P), classification dependent upon structure of the administered agent.
- II. Claim 8, drawn to a method of preventing implantation of an embryo in the uterine decidua endometrium, comprising administration of a differentiation factor selected from the group consisting of: TGF-beta, a TGF-beta analogue and an IGF-II antibody to inhibit interaction between IGF-II and CIM6P, classification dependent upon structure of recited the administered agent.
- III. Claim 9, drawn to a method of regulating differentiation and migration of stem cells, comprising administration of a differentiation factor selected from the group consisting of IGF-II, an IGF-II analogue and a TGF-beta antibody to promote interaction between IGF-II and CIM6P, classification dependent upon structure of the administered agent.

- IV. Claim 10, drawn to a method of promoting terminal differentiation of stem cells, comprising exposing said cells to reduced levels of IGF-II, thereby promoting activation of TGF-beta, classified, for example in class 435, subclass 325.
- V. Claim 11, drawn to a method of promoting stem cell division and stem cell migration, comprising exposing said cells to increased levels of IGF-II, thereby inhibiting the activation of TGF-beta, classified, for example, in class 435, subclass 325.
- IV. Claims 12, 13 and 14, drawn to methods of detecting the presence of a genetic polymorphism and/or a variable number of tandem repeats in the sequence of nucleotides in the IGF-II gene, classification dependent upon the type of assay used in recited methods.
- VII. Claim 15, drawn to a method of determining the ability of cytotrophoblast cells to differentiate and migrate, comprising measuring the amount of mRNA transcribed from the IGF-II gene in an embryo, classified, for example, in class 435, subclass 6.
- VIII. Claims 16 and 17, drawn to a method of determining the ability of cytotrophoblast cells to differentiate the method comprising measuring the amount of IGF-II protein in embryo or blood, classified, for example, in class 435, subclass 7.1.

Groups I-VIII are unrelated. Groups are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation,

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different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, Groups I-VIII utilize different methods. Although there are no provisions under the section for "Relationship of Groups" in M.P.E.P. § 806.05 for inventive groups that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct Groups for the following reasons:

Groups I and III are drawn to a method of administering a differentiation factor selected from a group consisting of IGF-II, and IGF-II analogue and a TGF-beta antibody to promote interaction between IGF-II and CIM6P, whereas Group II is drawn to a method of administering a differentiation factor selected from the group consisting of TGF-beta, a TGF-beta analogue and an IGF-II antibody to inhibit interaction between IGF-II and CIM6P, classification dependent upon recited "factor". Groups I and III are also distinct because while both are drawn to methods of administering a differentiation factor selected from a group consisting of IGF-II, and IGF-II analogue and a TGF-beta antibody to promote interaction between IGF-II and CIM6P, classification dependent upon structure of recited "factor", Group I is drawn to promoting cytotrophoblast differentiation and migration and/or promoting embryo implantation whereas Group III is drawn to the regulation of differentiation and migration of stem cells classification dependent upon structure of recited "factor", *i.e.*, Group I encompasses an *in vivo* method whereas Group III encompasses an *in vitro* method.

Groups I, III and IV-VIII are unrelated. Groups I and III are drawn to a method of administering a differentiation factor selected from a group consisting of IGF-II, and IGF-II analogue and a TGF-beta antibody to promote interaction between IGF-II and CIM6P,

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classification dependent upon structure of recited "factor", whereas Group IV is drawn to a method of exposing stem cells to reduced levels of IGF-II to promote the action of TGF-beta, classified, for example in class 435, subclass 325. Likewise, Groups I and III are different from Group V, which is drawn to a method comprising exposing stem cells to increased levels IGF-II in order to inhibit TGF-beta, classified, for example, in class 530 subclass 399. Groups I and III differ from Groups VI and VII, which are drawn to methods for screening for genetic polymorphisms and measuring mRNA, classification dependent upon the type of assay used in recited methods. Groups I and III differ from Group VIII, which is drawn to a method for measuring IGF-II levels in the blood, classification dependent upon the type of assay used in recited methods.

Groups II and IV-VIII are unrelated. Group II is different from Group IV because II is drawn to a method of administering a differentiation factor selected from the group consisting of TGF-beta, a TGF-beta analogue and an IGF-II antibody to inhibit interaction between IGF-II and CIM6P, classification dependent upon recited differentiation factor, whereas Group IV is drawn to a method of exposing stem cells to reduced levels of IGF-II to promote TGF-beta activity, classified in class 435, subclass 325. Likewise, Group II differs from Group V, which is drawn to a method comprising exposing stem cells to increased levels IGF-II in order to inhibit TGF-beta, classified in class 435, subclass 325. Group II differs from Groups VI and VII, which are drawn to a method for screening for genetic polymorphisms and measuring mRNA, classification dependent upon the assay used in the recited methods. Finally, Group II differs from

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Group VIII because, which is drawn to a method of measuring IGF-II in the blood, classification dependent upon the type of assay used in recited methods.

Group IV and Group V-VIII are unrelated. Group IV is drawn to a method of exposing stem cells to reduced levels of IGF-II, thereby promoting TGF-beta activity, classified, for example, in class 435, subclass 325, whereas Group V is drawn to a method of exposing stem cells to increased levels of IGF-II, thereby inhibiting TGF-beta activity, classified, for example in class 435, subclass 325. Although Groups IV and V have the same classification, Group II is drawn to a method of administering lower levels of IGF-II and Group V is drawn to administering higher levels of IGF-II. Likewise, Group IV differs from Groups VI and VII, which are drawn to methods for screening for genetic polymorphisms and measuring mRNA, classification dependent upon recited method. Finally, Group IV differs from Group VIII, which is drawn to a method of measuring IGF-II in the blood, classification dependent upon the type of assay used in the recited methods.

Group V is unrelated to Groups VI—VIII, because they are unrelated methods. Group V is drawn to a method of exposing stem cells to increased levels of IGF-II, classified, for example, in class 435, subclass 325, whereas Groups VI and VII are drawn to methods for screening for genetic polymorphisms and measuring mRNA, classification dependent upon recited method. Finally, Group V is unrelated to Group VIII, which is drawn to a method of measuring IGF-II in the blood, classification dependent upon the type of assay used in the recited methods.

Group VI, VII and VIII are unrelated methods. Groups VI and VII are drawn to methods for screening for genetic polymorphisms and measuring mRNA, classification dependent upon the type of assay used in the recited methods, whereas Group VIII is drawn to a method of measuring IGF-II in the blood, classification dependent upon the type of assay used in the recited methods. Finally, Groups VI and VII are unrelated methods, because VI is drawn to methods of detecting genetic polymorphisms and/or a variable number of tandem repeats in the sequence nucleotides in the IGF-II gene, classification dependent upon the assay used in the recited methods, whereas Group VIII is drawn to a method of measuring the IGF-II protein in the blood, classification dependent upon the type of assay used in the recited methods.

Although there are no provisions under the section for "Relationship of Groups" in M.P.E.P. § 806.05 for inventive groups that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct Groups for the aforementioned reasons. Therefore, search and examination of all of the methods in one patent application would be unduly burdensome since the searches are not coextensive, and since the methods require different reagents and method steps in order to achieve different goals.

This application contains claims directed to the following patentably distinct species of the claimed invention: differentiation factors. These differentiation factors are considered patentably distinct for the following reasons: they are different proteins with different structures and a different status in the art. Success with one does not render success with another obvious.

The species are as follows:

I. DIFFERENTIATION FACTORS

I-a. IGF-II

I-b. IGF-II analogue

I-c. IGF-II antibody

I-d. TGF-beta

I-e. TGF-beta analogue

I-f. TGF-beta antibody

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 3-7 and 10-17 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

This application contains claims directed to the following patentably distinct species of the claimed invention: The genes listed below are considered patentably distinct because they have different nucleotide sequences and encode different proteins with different activities and structures and a different status in the art. Success with one does not render success with another obvious.

The species are as follows:

II. GENES

- II-a. IGF-II
- II-b. Urokinase plasminogen activator
- II-c. Urokinase plasminogen activator receptor
- II-d. CIM6P (type IGF) receptor
- II-e. TGF-beta
- II-f. Plasminogen

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 1-12 and 14-17 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached 8:00-4:30, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached at 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christina Borgeest, Ph.D.
8/24/2005



ELIZABETH KEMMERER
PRIMARY EXAMINER